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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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07/402,450 09/01/89 MURAKAWA

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HM22/0830

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EXAMINER

MARSCHEL, A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED:

08/30/00

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No. 07/402,450	Applicant(s), Murakawa et al.
	Examiner Ardin Marschel	Group Art Unit 1631

Responsive to communication(s) filed on 8/8/96, 12/18/96, and 12/19/96

- This action is **FINAL**.
- Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claim

- Claim(s) 34-49 is/are pending in the application.
- ~~Other claims~~, Claim(s) 1-33 have been canceled. ~~Other claims~~
- Claim(s) \_\_\_\_\_ is/are allowed.
- Claim(s) 34-49 is/are rejected.
- Claim(s) \_\_\_\_\_ is/are objected to.
- Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All  Some\*  None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

The art unit designated for this application has changed.

Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

The result of an appeal to the Board of Interferences and Appeals was a REMAND back to the Examiner. Subsequently, applicants' submitted two amendments and requested an Interference with U.S. Patent Number 5,476,774 to Wang et al. These amendments have been entered and have canceled all claims that were previously under Appeal. This is in effect an abandonment of the appeal as discussed in the M.P.E.P. at § 1211.01, second paragraph. The clerk of the Board has been notified of the abandonment of the appeal. It is regretted that so much time has passed in the interim. However, in order to move prosecution forward in the instant application, it is deemed appropriate to respond to the issues set forth in said REMAND in preparation for ultimately resolving said potential Interference. It is noted that applicants have responded specifically to only one of the issues set forth in the REMAND. The response was a Petition to accept the instant application without Drawings. It is noted that this Petition has been granted. Further, in order to resolve these REMAND issues prosecution is hereby reopened. The Examiner will make every effort to expedite prosecution of this application.

In the Request for Interference, filed 12/18/96, applicants

proposed a count for the interference and indicated that this count should get benefit of at least the filing date of Serial Number 07/148,959; citing enabling support for the proposed count in that application at page 3, line 23, through page 5, line 11. Consideration of said pages 3-5 of Serial Number 07/148,959 reveals that an embodiment of the count is described therein directed to RT-PCR amplification of a reference RNA, which may be a maxigene, along with target HIV-1 virus RNA. The reference RNA serves as a control RNA, or internal standard, which may be utilized to candidate the starting viral HIV-1 RNA amount by comparing the amplification product amounts of both RCAS and knowing the initial amount of the reference RNA which was added to the amplification reaction mixture. It is noted that viral RNA is generically described elsewhere in application Serial Number 07/148,959. Even though this disclosure in application Serial Number 07/148,959 affords benefit for viral RNA and reference RNA embodiments of the proposed count, the disclosure of application Serial Number 07/148,959 does not contain other embodiments which are deemed to be included in the count such as the broader "target nucleic acid" or "internal standard nucleic acid segment" of said count. Such target nucleic acids are deemed to include DNA as well as RNA targets, possibly non-viral, including human or bacterial, for example. Similarly, the internal standard nucleic acid segment may be DNA as well as non-

viral etc. Thus, the benefit of application Serial Number 07/148,959 for certain embodiments of the count is a significant consideration, but said application does not provide complete enablement of the full scope of said count. Thus, the priority date for the count, as a whole, as well as instant claim 34 by comparison, for example, cannot be given any earlier than the filing date of the instant application which is 9/1/89. The other parent applications cited regarding the instant applications have also been reviewed as to possibly providing an earlier priority date. Application Serial Number 07/143,045 also is limited to viral RNA quantitation during RT-PCR via a control plasmid which may be RNA or DNA and which contains viral segments. An insert therein causes the PCR product of said plasmid amplification to be distinguishable by size from viral RNA amplification product. Thus, application Serial Number 07/143,045 also fails to provide a fully enabling disclosure for said count or instant claim 34; albeit providing benefit regarding what it does disclose. Consideration of the remaining parent applications; Serial Numbers 06/941,379 and 07/355,296 revealed that neither of them disclose the practice of a control or internal standard of any kind used during amplification reactions, such as discussed above, although certain plasmids per se, such as pGM92 and pGM93, are therein disclosed which may accord benefit for such limited embodiments of plasmid only. It

is also noted that the presently pending claims 34-49 all contain broader, or more generic, limitations regarding either target nucleic acid or control or internal control or standard nucleic acid as compared to those disclosed in the above listed parent applications. Thus, in summary, a fully enabled priority date for instant claims 34-49, as well as for the proposed count, cannot be given any earlier than that of the instant filing date of 9/1/89 regarding the instant application, although as noted above, certain more limited embodiments therein have benefit to applications Serial Numbers 07/143,045; 07/148,959; 07/355,296; and/or 06/941,379.

I.

CONSIDERATION OF THE ISSUES DESCRIBED IN SAID REMAND:

FIRST ISSUE: Consideration of a rejection under 35 U.S.C. § 102(e) over application Serial Number 07/180,740. It is firstly noted that application Serial Number 07/180,740 has been refiled as a file-wrapper-continuation. The file-wrapper-continuation Serial Number is 08/334,398 and has matured into U.S. Patent Number 5,622,820 to the single inventor given as John J. Rossi.

The abstract of Rossi (P/N 5,622,820) describes the simultaneous amplification of a marker sequence for detecting and identifying specific human nucleic acid sequences. In column 3, lines 28-46, co-amplification of internal standards is described. It is noted, however, that Rossi (P/N 5,622,820) does not teach

or suggest the quantitation of target nucleic acid via predetermining the amount of control nucleic acid and then comparing the amounts of the co-amplified nucleic acids. Only qualitative detection and/or identification practice is described in Rossi (P/N 5,622,820). It is noted that control plasmids, pGM92, pGM93, and pGM92+21 are disclosed as prepared in Rossi (P/N 5,622,820) in Example 1, starting in column 5 and further utilized in other Examples therein. Regarding the instant claim embodiments the control plasmids of concern are those of pGM92+21, pGM92, and pGM93, which are distinguishable by size or internal probe in a co-amplification method with the corresponding target HIV-1 nucleic acid. Comparison of the construction of pGM92+21 including insert and starting materials as given in Rossi (P/N 5,622,820) in the first paragraph of said Example 1 in column 5 with the construction of pGEM92 in application Serial Number 07/148,959; parent of the instant application reveals that the starting materials including the insert, KpnI insertion site, etc. appears to be identical albeit confusingly referred to as a 22 base pair insert in application Serial Number 07/148,959 and as a 21 nucleotide insert in Rossi (P/N 5,622,820). It is noted that the nucleotide sequences of at least one strand of both insert disclosures is identical. Thus, the benefit accorded to 07/148,959 prevents this plasmid from supporting a prior art based rejection. Also, plasmids pGM92 and

pGM93 were disclosed in application serial Number 06/941,379 which predates Rossi; Patent Number 5,622,820; thus also preventing a rejection based on these plasmids. In summary, the disclosure of application Serial Number 07/180,740 fails to support a rejection under 35 U.S.C. § 102(e). For completeness, the disclosure of application Serial Number 07/180,740 is also deemed to fail to support a rejection under 35 U.S.C. § 103(a) due to lacking target nucleic acid quantitation practice therein via internal standard co-amplification or other plasmids that may be utilized as internal controls.

## II.

### FURTHER CONSIDERATION OF THE ISSUES DESCRIBED IN THE REMAND:

SECOND ISSUE: Consideration of a provisional obviousness-type double-patenting rejection over application Serial Number 07/180,740. Since application Serial Number 07/180,740 as matured into U.S. Patent Number 5,622,820; this consideration will be regarding a non-provisional obviousness-type double patenting rejection over Rossi (P/N 5,622,820). As noted above the issue of obviousness has been already addressed as lacking a description of methods of quantitation via a internal control nucleic acid via co-amplification of the target and a predetermined amount of said internal control. Rossi (P/N 5,620,820) also lacks the claiming of any plasmids per se in the claims thereof. Thus, a prima facie case is lacking and thus

insufficient to support such an obviousness-type double-patenting rejection over Rossi (P/N 5,622,820).

III.

FURTHER CONSIDERATION OF THE ISSUES DESCRIBED IN THE REMAND:

THIRD ISSUE: Consideration of ambiguity and indefiniteness in all instant claims, especially claim 18. The cancellation of all claims under appeal including claim 18 is deemed to make this issue moot.

IV.

FURTHER CONSIDERATION OF THE ISSUES DESCRIBED IN THE REMAND:

FOURTH ISSUE: Consideration of prior art issues and effective filing dates for each of the instant claims. A discussion above as to both benefit as well as priority, or effective, dates for all of the instant claims is deemed to partially satisfy this issue. All of the presently pending claims fail to be given any earlier priority, or effective, date than the filing date of the instant application of 9/1/89. It is noted, however, that certain embodiments, as discussed above, are accorded benefit to certain applications which are parents of the instant application. Another concern within this issue is the relationship between the instant application and its parent applications. This has been corrected on the file cover and in the first paragraph of the instant specification as follows. Applicants are invited to review these relationships and provide

any corrections that may be necessary. The file cover summary is deemed to succinctly summarize these relationships and is repeated here:

THIS APPLN. IS A CIP OF 07/355,296 05/22/89 ABN  
AND A CIP OF 07/143,045 01/12/88 ABN  
AND A CIP OF 07/148,959 01/27/88 ABN  
WHEREIN 07/143,045 IS A CIP OF 06/941,379 ABN  
AND WHEREIN 07/355,296 IS A FWC OF 06/941,379 ABN

This issue then requests reevaluation of the prior art rejections. The previous prior art rejections are deemed moot regarding the appealed claims due to their cancellation. The presently pending claims are hereby reevaluated regarding such prior art issues. The prior art previously cited in support of prior art based rejections given as Mullis et al. (P/N 4,683,195); Ratner et al. (Nature 313:277[1985]); Hennighausen et al. (EMBO. J. 5(6):1367 [1986]); and Wathen et al. (J. Virology 41(2):462[1982]) upon reevaluation supports the below given prior art based rejections. However, the combination of these references as previously applied is deemed to fail to support a prior art rejection against the presently pending claims directed to mixtures of control or internal standard nucleic acids with target nucleic acids and primers which equally amplify both nucleic acids.

## FURTHER CONSIDERATION OF THE ISSUES DESCRIBED IN THE REMAND:

FIFTH ISSUE: Consideration of the issue of no drawings being filed with the instant application, even though the specification refers to drawings. This has been resolved as noted above via the granting of a petition to accept the instant application without drawings.

THE ABOVE COMPLETES CONSIDERATION OF THE ISSUES DESCRIBED IN THE REMAND:

For completeness regarding the prosecution of the instant application, the following newly applied rejections have been discovered as well as the below prior art issues which were mandated to be reevaluated as noted in the above discussion regarding said REMAND.

Claims 34-41 and 46-49 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instantly pending claims contain NEW MATTER due to being broader in scope than the disclosure as filed. The instant invention is described in the SUMMARY OF THE INVENTION section as being directed to the determination of the presence or absence of

viral RNA. No other target RNA or target DNA has been instantly disclosed. It is noted that viral DNA amplification within the instant method is an embodiment thereof as disclosed in application Serial Number 07/143,045 on page 8, lines 15-18, which has been incorporated by reference into the instant application. Thus, the instant claims which are generically broad in citing target nucleic acid contains NEW MATTER as being directed to target nucleic acid which is deemed to include non-viral RNA or DNA. This broader scope is NEW MATTER.

Claims 36, 40, and 44 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 lacks a limitation that the resultant products of amplification of the control sequences versus the target sequences are distinguishable either by size or by use of an internal oligonucleotide probe. It is noted that all of the control sequences or internal standards that are described in the instant specification are quantitated either via size separation of amplification products thereof or via hybridization to an internal oligonucleotide probe. Neither of these capabilities are limitations of instant claim 36 and this causes this claim, was well as claims 40 and 44 via dependence from claim 36, to not be commensurate in scope with the specification as required.

Claim 49 is rejected under 35 U.S.C. § 135(b) over Wang et al. (P/N 5,219,727).

Wang et al. (P/N 5,219,727) was issued on Jun. 15, 1993. Claim 1 of Wang et al. (P/N 5,219,727) is directed to a method of amplification which utilizes an internal standard or control sequence for quantitation of target nucleic acid wherein the same primers will amplify both the target nucleic acid as well as the internal standard or control sequence. It is noted that the process or method claims in the instant application had previously been limited to processes for the detection or quantitation of viral RNA only. Claim 49, as filed on 12/19/96, is not so limited but rather generic regarding target nucleic acid. This increased scope supports this rejection under 35 U.S.C. § 135(b) as the embodiments directed to non-viral RNA target nucleic acid or DNA (any target) are not filed within the required one year after issuance of said Wang et al. Patent Number 5,219,727.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an

application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 36, 37, 40, 41, and 48 are rejected under 35 U.S.C. § 102(b) and (e) as being clearly anticipated by Mullis et al. (P/N 4,683,195).

Mullis et al. starting at column 21, line 22, discloses Example 2 wherein PCR amplification primers are synthesized for pBR328 segment amplification. In column 22, line 63, through column 23, line 56, various reaction mixtures are prepared using these same primers with different target nucleic acids. It is noted that Lanes 2 and 3 containing amplified pBR328:HbA and pBR328:HbS, respectively, as shown in Figure 3 are amplified with the same primers and serve as control sequences compared to the MstII restriction enzyme digested plasmids (Lanes 4 and 5) which are attempted to be amplified in Lane 4 but does not due to the MstII restriction enzyme cut of that plasmid, versus the result shown in Lane 5 which prevents the MstII cut and yields an amplification product. In column 22, line 66, through column 23, line 3, predetermined amounts of control nucleic acid are disclosed as being added to their respective reaction mixtures. Thus, the components of the kit of instant claim 36 are disclosed as these various components. Control sequence and primers for amplification thereof which can also prime to amplify other

target nucleic acids. It is inherently required that the disclosure of adding these components occurs from separate individual containers. It is additionally noted that the quantitation usage wording in instant claim 36 is deemed a product by process limitation which does not prevent this rejection in that the product may also be used in the method of Mullis et al. even though it also has the use for quantitation methodology. Lastly, it is noted that instant claims 40 and 41 were included as rejected hereinunder because these claims limit the control sequence to maxigenes. In order to understand what is meant thereby the definition of maxigene in the specification was considered on page 6, lines 19-21, wherein it is defined as a multi-base pair insert or deletion of at least 20 nucleotides from a unique site. The HbA and HbS inserts described above into the pBR328 plasmid are clearly unique sites from alleles of sickle cell or normal hemoglobin sequence and each are 1.9 kb in length. Thus, these inserts meet the definition of maxigenes as given in the instant specification thus supporting the rejection of instant claims 40 and 41 hereinunder.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 36 and 40 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mullis et al. (P/N 4,683,195); taken in view of the kit description in the 1988 Stratagene Catalog.

Mullis et al. has been described above as disclosing the primers and control nucleic acids of the instant claims 36 and 40. Mullis et al. may be interpreted as not disclosing a kit per se.

The 1988 Stratagene Catalog at page 39 motivates and suggests that the assemblage of materials into kits which may be pre-mixed for the benefits therein cited such as availability and quality testing etc. It is noted that kits are also well known in Biochemical work with either individual or mixed components

ready for use.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to assemble the components for use in the Mullis et al. Example 2 reactions in order to perform the demonstration therein of various amplification results regarding Sickle Cell Anemia detection as motivated and suggested by the 1988 Stratagene Catalog page 39 thus resulting in the practice of the kits of instant claims 36 and 40. It is lastly noted that instant claim 36 does not clearly define what is in each of the individual containers. That is, the individual containers of claims 36 and 40 may be reasonably interpreted as containing both the control sequence as well as the primer pair either in one container or in separate containers with other containers for other amplification method components such as polymerase, buffer, etc. which may be used in various types of target nucleic acid quantitative methods.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619

(CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 34-45 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 31-42 of copending application Serial No. 08/769,584. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being

unpatentable over claims 31-42 of copending application Serial No. 08/769,584. Although the conflicting claims are not identical, they are not patentably distinct from each other because each respective sets of claims include common embodiments of reaction mixtures and plasmids which are control standards which are usable to form amplification products which are distinguishable by size. Given the process steps cited in the composition claims instant claim 49 is included as an obvious use therefore.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Prior to further processing of the instant application regarding the Request for Interference, the above issues must be addressed.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 25, 2000

*Ardin H. Marschel*  
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